18. (Amended) ~~A method of immunizing~~ [an adult] a human, comprising:

a) providing: i) a human [an adult with symptoms of autoimmune disease], and ii) an immunizing preparation comprising myelin basic protein [an Autoimmune Target Antigen] and Incomplete Freund's Adjuvant;

b) immunizing said [adult] human with said immunizing preparation;

c) obtaining a primary cell population from said immunized [adult] human comprising T cells capable of secreting cytokines;

d) adding said primary cell population to said microwell comprising a hydrophobic membrane having a first cytokine binding ligand, under conditions such that said T cell secretes a cytokine that binds to said first cytokine binding ligand; and

e) detecting said secreted T cell cytokine.

REMARKS

Claims 1-3 and 18-19 are at issue and stand rejected. Claims 3 and 18 have been hereby cancelled.For clarity, the Examiner's rejections are set forth below:

(1) The Claims are rejected under 35 U.S.C. § 112, first paragraph as not enabled.

(2) The Claims are rejected under 35 U.S.C. § 103 as being obvious.

Applicants believe that the following remarks traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

(1) The Claims Are Enabled

The Claims stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that "[t]he state of the art is such that is unpredictable from the mouse data disclosed in the specification as to how the instant invention could be used for the treatment of disease *in vivo* in humans" (Office Action, page 2).

Applicants cannot agree. First, as noted previously, the animal model is an autoimmune model having nothing to do with cancer and the purported problems with animal models in cancer discussed by Osband *et al.* Second, the Examiner's concerns regarding

proteolysis and half-life have no relevancy to the field of immunizations and vaccinations. Since both of these arguments were provided in the previous response, they need not be repeated in depth here.

In the new Office Action, the Examiner has cited Tisch, arguing that the reference makes it "unclear whether the EAE model is a suitable model for human MS." (Office Action, page 4). Applicants respond by noting that the Tisch reference only questions whether the model predicts more than **protective** benefits of treatment:

> "The most critical factor is whether the therapy can be used to **treat** an ongoing autoimmune response or whether it is effective only in term of **prevention**."

(*See* Tisch , page 437, middle column at bottom, emphasis added). Tisch does not question the fact that the EAE is a good model to determine protective therapies.

Without taking issue with Tisch regarding treatment, and without waiving the right to prosecute treatment claims (and broader claims) in the future, but to further the prosecution, applicants have amended claims 1 and 18 to specify that 1) the immunization is with myelin basic protein, and 2) the immunization is protective against MS. The Claim does not specify whether the human has symptoms or not. It is not contemplated that the Claim is directed at protecting against autoimmunity.

With these amendments, it is submitted that the enablement rejection should be withdrawn. The claims are not specific to the results from the animal model. No claim is made that the immunization will reduce existing symptoms. Moreover, the claim breadth issue raised by the Examiner is rendered moot by the limitation to myelin basic protein.[1]

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[1] Applicants stress that the Examiner's characterization of the data in the specification is in error. The Examiner argues that "there is no murine data . . . other than the specific example of murine EAE treated with MBP or EAE." (Office Action, page 3 at the bottom). The Examiner has apparently overlooked the data of Example 4 wherein mice were tested with RTA/IFA and the results permitted the conclusion that "the rules established for EAE (see above) also apply for the autoimmune model of interstitial nephritis." (see page 18). While the Examiner has failed to consider this data which confirms the generality of the present invention (a generality which will be pursued in the future for other claims), applicants have elected at this time (in view of the restriction requirement) to further the prosecution by limiting the claims in the manner described above.

(2) The Claims Are Nonobvious.

Claim 1 was rejected under 35 U.S.C. § 103 as being obvious in view of Tobin. However, since Claim 1 has been amended to specify myelin basic protein, the teachings of Tobin are largely irrelevant. Moreover, the Examiner has argued against the generality of the present invention, citing negative results of Cohen (*see* Office Action, page 3). Thus, Tobin cannot be used as a general teaching for an obviousness rejection against the present (amended) claims:

> "We must not here consider a reference in a vacuum, but against the background of the other references of record which may disprove theories and speculation in the reference, or reveal previously undiscovered or unappreciated problems. The question in a § 103 case is what the references would *collectively suggest* to one of ordinary skill in the art."

Application of Ehrreich, 590 F.2d 902, 908-09, 200 USPQ 504, 509-510 (C.C.P.A. 1979) (emphasis in the original).

The Namikawa *et al.* reference is also cited against Claim 1. The Examiner argues that "Namikawa *et al.* teach that immunization with MBP in IFA ... prevents EAE in rats." (Office Action, page 5). Applicants cannot agree with the Examiner's characterization of the reference. As noted previously, the teachings of this reference suggest that BP in IFA will cause mild EAE symptoms. Moreover, the protective effects were not complete. The reference notes that "two of the nine rats pretreated with BP/IFA developed clinical signs of EAE after challenge." (p. 933, left-hand column, second sentence). The Examiner is not free to ignore these teachings.

Claims 2 and 18 contain specific method steps. The Examiner combines the above-cited art with Goodwin (importantly, no basis is cited for making the combination). The Goodwin reference does teach the measurement of cytokines at column 10. However, **none** of the references teach the advantages of a *hydrophobic* membrane having a cytokine binding ligand.

The Examiner's answer to this problem is to note that hydrophobic membranes are known (Office Action, page 6). This argument does not established a *prima facie* case of obviousness. The mere fact that an element is known does not support an obviousness argument:

> "That all elements of an invention may have been old (the normal situation), or some old and some new, or all new, is however, simply irrelevant. Virtually all inventions are combinations and virtually all are combinations of old elements."

Intel Corp. v. United States Int'l Trade Comm'n, 946 F.2d 821, 842, 20 USPQ2d 1161, 1179 (Fed. Cir. 1991) [Quoting from *Environmental Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983)].

Indeed, the use of a hydrophobic membrane has advantages (e.g. lower background) over the commonly used hydrophilic membranes. None of these advantages are disclosed in the art cited. Thus, Claims 2 and 18 should be allowed.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicant's claims as amended should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (617) 354-5455.

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